NavMed 369

UNITED STATES NAVY

MEDICAL NEWS LETTER

Editor - Captain F. W. Farrar, MC, USN

Vol. 12 Friday, 30 July 1948 No. 3

TABLE OF CONTENTS

Circular Letters:

* * * * * *

* * * * *

Administration of Chloromycetin to Normal Human Subjects: This report summarizes the observations on three normal male human volunteers who were given Chloromycetin.

The oral route was selected for the administration of the drug, not only because of its convenience, but also because of experimental evidence which indicated that the drug was effective by this route in treating infected mice. Tablets containing 0.1 Gm. amounts of crystalline Chloromycetin were supplied for the trial by the Research Laboratories of Parke, Davis, and Company.

Levels of Chloromycetin in blood and urine were determined in samples collected at intervals throughout the study. A modification of the method of Joslyn and Galbraith which employs inhibition of growth of Shigella paradysenteriae (Sonne) was used for these microbiological assays. Blood and urine specimens taken for such assays were obtained in the following sequence: the patient voided, was bled, and then the urine sample for assay was collected within a few minutes. In addition, urine was collected for 24-hour periods in order to permit estimation of the total daily urinary excretion of Chloromycetin.

In the first test 2 of the subjects received a prolonged course of Chloromycetin beginning with a single dose of 1.0 Gm. which was followed by 1.0 Gm. daily for 10 days; the latter was given in divided doses of 0.2 Gm. every 4 hours except at 4:00 a.m. The peak values for both blood and urine were recorded for the first specimen collected at 2 hours after the initial dose. Subsequently, the blood levels fell steadily in both subjects and detectable amounts of drug were not demonstrable at 8 hours or thereafter. The levels of the drug in the urine were approximately 200 γ per c.c. at 2 hours; they fell to approximately 50 γ per c.c. at 8 hours and remained at about that level for the next 10 days of treatment. During and immediately following the test no significant changes occurred in the blood of either subject as revealed by determination of hemoglobin, erythrocytes, and leukocytes and by examination of blood smears. Urinalysis on the third day of therapy showed no abnormalities.

In a second test one of the volunteers from the first experiment and another subject received an initial dose of 2.0 Gm. followed in 8 hours by a single 0.5-Gm. dose. Relatively high levels of drug were found in the blood of both volunteers only 30 minutes after the antibiotic was first given by mouth; furthermore, at this time drug was already present in the urine in appreciable amounts. The blood levels were still well above 10 γ per c.c. at 2 hours and were above 5 γ per c.c. at the end of 8 hours. Urinary drug levels in the subjects were at their maxima at 2 hours, reaching values of 670 γ per c.c. in one and 380 γ per c.c. in the other. The amounts diminished rapidly in successive samples and dropped to about 10 γ per c.c. at 8 hours.

Approximately 10 percent of the total amount of Chloromycetin given daily was recovered in an active form in the urine of both groups of volunteers.

No symptoms or signs of toxic effects attributable to the drug were observed by the 3 volunteer physicians either during the treatment or subsequently.

These limited trials indicate that Chloromycetin can be given orally to normal adult males in single doses of 2.0 Gm., or in daily doses of 1.0 Gm. for 10 days without untoward reactions. The presence of appreciable amounts of drug in the blood and urine of volunteers 30 minutes after oral administration of Chloromycetin indicates that the antibiotic is absorbed rapidly from the gastrointestinal tract of man. Excretion or inactivation of the drug occurs rather rapidly; hence, in order to maintain appreciable levels of the antibiotic in the blood, it should be administered frequently. (Proc. Soc. Exper. Biol. and Med., May '48 - H. L. Ley, Jr. et al.)

* * * * * *

Chloromycetin in the Treatment of Patients with Typhus Fever: Recent reports indicate that Chloromycetin is effective in the treatment of experimental infections caused by Rickettsia prowazeki and Rickettsia mooseri as well as other rickettsial and viral agents. Studies have shown that Chloromycetin can be given to normal men without untoward effects and that the levels of the drug in the blood and urine of treated persons can be followed. This paper summarizes the information gained from the study of a small group of patients with typhus fever who were treated with Chloromycetin.

The patients studied in the current investigation were hospitalized in Mexico City. Crystalline Chloromycetin prepared in 0.1 Gm. tablets for oral administration was supplied by the Research Laboratories of Parke, Davis, and Company. Chloromycetin levels in the blood and urine of patients were determined by a modification of the method of Joslyn and Galbraith. Specific rickettsial complement-fixation and agglutination tests were performed according to the standard procedure of the U. S. Army Medical Department Research and Graduate School. The results of the Weil-Felix tests recorded on the graphs were done by the technic employed at the School; comparative studies in which sera were tested with proteus antigens prepared at the School and at the Institute by the technics employed in both laboratories gave comparable results. Leon's technic, for the demonstration of specific typhus antigen in the urine of early typhus patients, was employed in two of the treated patients and found to be positive in each instance.

Five patients with typhus fever were treated with Chloromycetin. More complete and definitive information was obtained on the 3 adults than on the 2 children; therefore, each of the former will be discussed in some detail and the latter will be presented briefly. The first patient, A. F., received an initial dose of 1.0 Gm. of the drug by mouth on the morning of the fifth day of illness and subsequently was given 0.2 Gm. every 4 hours throughout the next 3 days and part of the fourth day. The levels of Chloromycetin ranged around values of 5γ per ml. in the blood and 100γ per ml. in the urine. During the course of therapy the white blood cells

diminished progressively from 5,700 on the fifth day of disease to 2,900 on the eighth day. At this point the possible relationship between the drug and the leukopenia was considered. This idea was dismissed on the ninth day when the patient's white cell count rose to 6,900 while he was still on therapy. There was a reduction in the hemoglobin content of the blood between the fifth and seventh days; however, it was assumed that the patient actually had a moderate anemia at the onset of his illness and that the initial value of 12.2 Gm. was dependent upon hemoconcentration during the period of high fever. Serological data indicated that this patient had epidemic typhus. It is difficult to say how much patient A. F. was benefited by treatment with Chloromycetin. In retrospect, it was the impression of the group that this patient had been treated with doses of drug which were too small and that the antibiotic had been given for too short a period of time.

Patient R. L. had lived with patient A. F. Her disease, characterized initially by feverishness and headache, began on the day that patient A. F. was hospitalized. She had a cutaneous rash when admitted on the fifth day of her illness. Leon's test performed with a sample of her urine taken on the morning of the sixth day gave a positive reaction; a Weil-Felix test on serum obtained at this time was positive at a dilution of 1/40. The patient was given 2.0 Gm. of Chloromycetin at noon on the sixth day. At 1:00 p. m. she vomited and was promptly given 0.5 Gm. of Chloromycetin. This was followed by administration of 0.2 Gm. every 4 hours until the morning of the 13th day of her illness. The blood level of Chloromycetin reached 11.5 γ per ml. on the morning of the second day of treatment and remained near that level the next day, but subsequently dropped to a value of about one γ per ml. The urinary level ranged around 100 γ per ml. for several days, but reached 220 γ per ml. on the seventh day of treatment. The abrupt return of the patient's temperature and pulse to the normal range following administration of Chloromycetin at first led to the suspicion that she did not have typhus, but the serological data subsequently indicated that this woman was infected with R. prowazeki. Other clinical abnormalities abated more slowly than the fever; thus, on the morning of the seventh day when the temperature was 37° C., the rash remained unchanged, the patient complained of headache and insomnia, and she still had flushed facies and conjunctival injection, as well as slight tremor of the tongue. The following day the patient was much improved and on the ninth day after onset she had no complaints, the rash was fading, and the conjunctival injection as well as the tremor and dryness of the tongue were gone. On the 12th day the patient was cheerful and sat up in bed. She was discharged from the hospital on the 15th day after onset.

Patient D.G.M. was admitted to the hospital on the seventh day of an illness which appeared typical of typhus fever. He was extremely ill with a fever of 40° C. and had an extensive, discrete macular rash which was not yet hemorrhagic. The Weil-Felix test at this time was positive at a dilution of 1/640. At 1:00 p. m. on the eighth day of illness the patient was given 1.5 Gm. of Chloromycetin by mouth; this was repeated at 2:00 p. m. Subsequently, he received 0.2 Gm. every 2 hours day and night until the morning of the 11th day at which time the dosage

was reduced to 0.2 Gm. every 3 hours. The following day the drug was further reduced to 0.2 Gm. every 4 hours and the drug was discontinued on the morning of the 14th day. The blood level of Chloromycetin rose rapidly and reached a value of 40.5 γ per ml. at 8:00 a. m. on the morning of the second day of therapy: similarly the urinary level had risen progressively and reached a value of 400 γ per ml. at this time. During the next few days the blood level of drug ranged between 10 and 5 γ per ml. and the urine around a value of 100 γ per ml. Although the temperature dropped to 38° C. on the morning after therapy was begun, the semidelirium continued, the rash had become petechial in some areas, the conjunctivae were still markedly injected, and fine tremors of the tongue and extended fingers continued unabated; that afternoon the temperature returned to 40° C. On the morning of the tenth day the temperature was 37.5° C., the cutaneous lesions were unchanged, and delirium still persisted. Despite the possibility that the drug therapy might have been contributing to the delirium, Chloromycetin was continued. The next day the patient's temperature was normal and he was lucid; therefore, it was assumed that the drug had not played any role in producing the patient's confused mental state. The improvement from the 11th day was obvious. It was the impression of the group that this had been an extremely severe case of epidemic typhus, in which the prognosis on the eighth day was ominous, and in which recovery was more rapid than one would have expected.

Of the two children treated with Chloromycetin during this study, one had murine typhus and the other epidemic typhus. In general, the children received orally amounts of drug which were comparable to that given to adult patients on the basis of body weight. It was the impression that Chloromycetin therapy produced no untoward effects in these children and may have been of some benefit. Typhus fever in children is generally so mild that evaluation of any therapeutic agent is extremely difficult even when large numbers of cases are investigated.

On the basis of these limited observations, it may be concluded that the administration of Chloromycetin to patients with typhus fever is a relatively safe procedure. Furthermore, the chemotherapeutic effect believed to have been obtained in the few patients treated seemed sufficiently encouraging to warrant further tests with the drug. It is suggested that Chloromycetin be employed in oral treatment of the next group of patients to be studied according to the following schedule; an initial dose of 40 mg. per kilo body weight followed by a total daily dose of 35 mg. per kilo body weight, given in divided amounts at 2-hour intervals, until obvious improvement in the patient's condition is noted; subsequently, maintenance dose of 20 mg. per kilo body weight per day given in divided amounts at 4-hour intervals, until the 13th or 14th day after onset. (Proc. Soc. Exper. Biol. and Med., May '48 - J. E. Smadel et al.)

* * * * * *

Streptomycin in Tuberculosis: Shortly after it was shown that streptomycin inhibited the growth of Mycobacterium tuberculosis, Feldman and Hinshaw applied the drug to tuberculous guinea-pigs with favorable results and were able to report its salutary effects on certain types of tuberculosis in human beings. A few individual investigators, the Veterans Administration and the Army and Navy, the United States Public Health Service, and the Therapy Committee of the American Trudeau Society have, altogether, studied the effects of the drug in about 2,000 patients, with results which suggest the following deductions:

(1) Streptomycin should be tried in all cases of miliary tuberculosis, for more than half of such patients will be alive, and a substantial number of them will be free from clinical, x-ray, or laboratory signs of disease from 6 to 12 months after discontinuation of the drug.

(2) The use of the drug in tuberculous meningitis is mandatory, for about one fourth of all patients have survived for from 6 to 12 months after treatment, and the majority of these are free from detectable signs of tuberculosis.

(3) Acute tuberculous pneumonia or exudative (fresh) tuberculous disease of the lungs will usually show recession, with notable clearing of the lungs demonstrable roentgenographically within a few weeks. Tubercle bacilli disappear from the sputum in about half of these cases. Such patients, however, need still further sanatorium care.

(4) Extrapulmonary tuberculosis is under detailed study, but already it appears that tuberculous laryngitis and bronchitis are benefited by the use of streptomycin in about 85 percent of cases, even though the parent lesion in the lungs may show no improvement. Tuberculous enteritis and cystitis likewise tend to improve. In fact, in areas in which the disease affects the epithelial surfaces, results are generally good; cutaneous sinuses are benefited. However, tuberculosis of the osseous and genito-urinary systems needs further study.

(5) Streptomycin is used profitably at times to enhance the patient's chances from collapse therapy and as a prophylactic in surgical treatment, particularly pulmonary resection.

In the face of these relatively good results, however, the average case of fibrocavernous tuberculosis has been found as yet to respond poorly to streptomycin; this type represents three fourths of all cases of the disease. It is still under intensive study. Moreover, the toxicity of the drug and the development of streptomycin-fastness by M. tuberculosis are disturbing factors.

In the early experience with this drug, with large doses of 2, 3, or even 5 Gm. a day, toxic symptoms were very common. Even with a standard dose of 1.8 Gm., vertigo developed in approximately 92 percent of one large series of

patients. McDermott, among others, has pointed out the common indices of toxicity. Vestibular dysfunction predominates, characterized by vertigo, dizziness, headache, and nausea, some of which are present to some degree in almost all patients who take large doses. Vertigo occurs in 20 percent or more of those receiving 1.0 Gm. per day, which is now the prevailing dose. It may be permanent. Deafness, partial or complete, has been observed. It occurs rarely except when the drug is applied intrathecally for tuberculous meningitis or (less often) in persons with impaired renal function who receive large doses. Further damage to the kidneys may occur in this latter group, a fact which indicates the propriety of determining the condition of the urinary tract prior to administration of the drug. In patients with already lowered renal function, blood levels may become high and various toxic symptoms ensue. Other indications of toxicity are anaphylactic manifestations - fever, itching, dermatitis and eosinophilia - and agranulocytosis. The latter appears in less than 1 percent of cases and is usually an indication for prompt discontinuation of treatment.

The development of streptomycin resistance by M. tuberculosis, occurring rather regularly, presents a serious obstacle in the use of the drug. Whether this represents biological adjustment to a new environment or the survival and increasing preponderance of natively resistant bacilli in the diseased body is not known. Once it becomes manifest, however, it appears to persist, and resistant strains have been maintained in culture for considerably over a year and have been passed through animals without reverting.

The production of resistant strains should be a serious consideration in the therapeutic use of streptomycin in patients manifestly unlikely to recover because the spread of such strains could conceivably become a grave public health hazard. To obviate this, careful selection of cases and frequent in vitro examination after the first 6 weeks of treatment are indicated, but continuation of the drug beyond 6 weeks is to be discouraged.

In general, streptomycin should be withheld in cases of minimal tuberculosis and in those in which conventional treatment offers reasonable prospect of good result. It provides an excellent medium of treatment for certain types of tuberculosis, but it should be used in association with accepted therapeutic measures and not as a substitute for them. A tendency is at present developing to use the drug only as an adjunct rather than as a definitive treatment in all types of tuberculosis except the miliary and meningitic forms, and to apply it briefly for 3, 4, or 6 weeks at the most opportune time with other appropriate therapy. (Editorial, Radiology, June '48 - H. S. Willis)

* * * * * *

The Effect of Dicoumarol on the Heart in Experimental Acute Coronary Occlusion: This study was undertaken to learn whether adverse myocardial changes might result from the use of dicoumarol to prevent thrombo-embolic phenomena and propagation of the thrombus following coronary thrombosis.

The experimental approach to this problem was considered to offer the following advantages: (1) The site of occlusion could be chosen, and, therefore, a more uniform situation would be offered for comparative studies. (2) The mechanism and rate of occlusion under experimental conditions would be more uniform. (3) The effect of the drug on the myocardium could be studied accurately by sacrificing the animal and examining the heart at stated intervals following occlusion and administration of anticoagulants.

For the purposes of the study, in 31 dogs the left anterior descending coronary artery or a major branch was ligated. The effect of the oral administration of dicoumarol on the myocardium and coronary arteries was studied in 14 animals. In three dogs, heparin was administered several hours postoperatively until the effect of dicoumarol was apparent. Fifteen dogs served as a control group.

It was observed that the incidence and magnitude of hemorrhagic extravasations on the endocardium and pericardium were the same in the animals in the treated and untreated groups. Moreover, the incidence and magnitude of miliary hemorrhages observed on microscopic examination of the heart muscle were similar in the dicoumarolized and control animals. In a small group of dogs in which sufficient dicoumarol was administered to elevate the prothrombin time to levels as high as 132 seconds, no increase in the hemorrhagic phenomena was observed in the myocardium. The size of the infarcts in the dicoumarol-treated and untreated animals showed no significant differences. The size of the infarcts was that which could be anticipated on the basis of the artery occluded. There were no apparent differences in the reparative processes in the hearts of the dicoumarol-treated and the control animals. Thrombotic occlusions of the smaller arteries were found within the infarcted area in dogs receiving dicoumarol approximately as often as in the untreated group. No thrombi were found in the region of the tie below the point of occlusion. In one instance, in an untreated animal, a thrombus was found in the region of the tie above the point of occlusion. No mural thrombi were found in the auricles or ventricles in the treated or in the untreated animals. The development of collateral anastomotic channels between the coronary arteries was the same in both groups. On or about the fourth day, unmistakable evidences of collateral vessels between the left anterior descending branch distal to the tie and the circumflex branch of the left coronary artery were observed. On and after the sixth day of survival, the magnitude of these anastomotic vessels was markedly increased.

The results of this investigation reveal that dicoumarol produces no adverse effects on the myocardium of dogs which retard the healing process or the development of collateral circulation in experimentally produced myocardial infarction. (Am. Heart J., July '48 - H. L. Blumgart et al.)

* * * * * *

Neurosyphilis in the Tropics: Initial experiences in Trinidad, B.W.I., led the author to discount the belief of many physicians that neurosyphilis is comparatively rare in that area. The lack of adequate diagnostic

facilities, both clinical and laboratory, seemed responsible for this belief. Reports from other tropical areas indicate that similar deficiencies may account for the supposedly low incidence of neurosyphilis elsewhere in the tropics.

The author undertook a study to determine the percentage of patients with neurosyphilis among those who were known to have syphilis in this area. The patients were an unselected group garnered largely through a program of mass blood testing. The presence of yaws was a complicating factor. In the presence of a positive serologic test for syphilis (STS), the following criteria were used to make a diagnosis of yaws and to exclude syphilis:

(a) The presence of typical active lesions of yaws.
(b) The presence of typical scars of yaws with a low-titer serological test for syphilis (usually less than 8 Eagle units), a history of residence in an endemic yaws area, and a history of treatment for yaws in childhood.
(c) A cerebrospinal fluid showing a negative serological test for syphilis.

When any doubt existed, a diagnosis of syphilis was made. A number of cases of inactive yaws were undoubtedly called syphilitic because of this policy. Of 108 patients whose cases were given an initial clinical diagnosis of inactive or tertiary yaws, only two showed CSF abnormalities; and of these two, one almost certainly had syphilis rather than or in addition to yaws.

The procedure followed in this study was to perform a routine serological test for syphilis. If positive, it was repeated; and if the second test was positive, the patient was put through a diagnostic clinic for a thorough physical examination. In most instances the spinal fluid examination could not be performed until after antisyphilitic therapy had been started. This may have caused a few initially positive spinal fluids (which became negative under treatment) to be missed. The Eagle and Kahn tests were used for the blood specimens. A cell count, the Pandy test for determination of protein, the Eagle modification of the Wassermann compliment-fixation test, and an Eagle flocculation test were performed on all cerebrospinal fluids. Colloidal gold curves were not done.

The cerebrospinal fluid examinations on 1,028 patients were reviewed. The results are presented in the table below.

The clinical records of 527 of the total patients were studied, and the CSF findings were correlated with their final diagnoses.

There were included among the 527 cases 107 patients whose final diagnosis was inactive yaws and 3 patients with active osseous and cutaneous yaws. A total of 110 patients (20.9 percent) of the group thus had a final diagnosis of yaws. The incidence of active yaws is low because patients

Group	Number of cases	Percent of total
a. Normal fluids [1]	823	80.0
b. Fluids showing increased cell counts (6 to 150 cells per mm.[3]) but no other abnormalities	52	5.1
Positive fluids [2]	153	14.9
c. Showing minimal to moderate changes	126	12.3
d. Showing marked changes	27	2.6
Total	1,028	100.0

[1] 4 cases of tabes dorsalis diagnosed in this group.
[2] As defined in this study.

with typical cases of active yaws were placed on treatment as soon as the diagnosis was made and did not have CSF examinations routinely. The author's policy of considering a case syphilitic when in doubt makes 20 percent a conservative estimate of the amount of yaws among patients with a positive serological test for syphilis. By eliminating 110 of the original 527 patients, 417 patients remained who were considered syphilitic. Of the 417 cases, 82, or 19.7 percent, were neurosyphilitic, as shown in the table below.

Diagnosis	Number of cases	Percent of total cases
Asymptomatic neurosyphilis	48	9.1
Symptomatic neurosyphilis	34	6.4
Tabes dorsalis	13	2.5
Taboparesis	1	.2
Paresis	5	.9
Meningovascular	5	.9
Vascular	2	.4
Optic atrophy (without other clinical evidence of neurosyphilis)	8	1.5
Total neurosyphilis	82	15.5

The distribution of races among the neurosyphilitics was essentially the same as the racial distribution among the entire group under study. The population of Trinidad is cosmopolitan, and the largest racial group is Negro. There is much intermarriage between races, but most of the individuals termed "mixed" are predominantly Negro.

It is concluded that neurosyphilis is not a rarity in the tropics. The application of modern clinical and laboratory methods in other areas will undoubtedly confirm this finding of a neurosyphilis rate of 20 percent in unselected syphilitics. It may be that symptomatic neurosyphilis tends to be a less severe affliction among natives of the tropics than among North Americans and Europeans. However, severe neurosyphilis is frequent enough to warrant early attention to the cerebrospinal fluid in all cases of syphilis. The severity of neurosyphilis may be somewhat tempered by the presence of endemic malaria. Malaria incidence rates of from 20 to 80 percent existed in some areas from which these patients were drawn. (J. VD Information, July '48 - M. J. Cook)

* * * * * *

The Technic of the Tissue Spread Method for Demonstrating Donovan Bodies: The Journal of Venereal Disease Information, Volume 29, Number 7, July 1948, contains an article giving detailed information for obtaining, preparing, and staining for microscopic examination the tissue spread specimens for the demonstration of Donovan bodies of granuloma inguinale. The technic given has been used for several years in the laboratories of the U. S. Public Health Service Medical Center, Hot Springs, Arkansas. The article was prepared by Mr. G. R. Cannefax, Bacteriologist, USPHS, and Laboratory Director, USPHS Medical Center, Hot Springs National Park, Arkansas, as a result of many requests for concise information relating to laboratory technics which aid in the diagnosis of granuloma inguinale. Microscopic slides, with Donovan bodies encircled for rapid location and demonstration, are being accumulated and are available through the author. Reprints of the article will also be ready for distribution within a few weeks after publication of this issue of the Journal of Venereal Disease Information. Requests for both reprints and slides should be addressed to Mr. Cannefax.

Methods of Rat Destruction: According to O'Connor the rodenticides in common use all have the disadvantage that they are rapidly acting and produce acute symptoms of poisoning even when eaten in sublethal doses. This produces the troublesome condition of "bait shyness" in the rat colony and makes 100 percent eradication difficult, even when prebaiting is used. He has therefore been studying the use of dicoumarol which acts slowly. Dicoumarol is the active compound found in spoiled sweet clover which has long been known to produce a fatal hemorrhagic disease in cattle when eaten by them. The average fatal dose for albino rats weighing 250 Gm. is 28 mg. if taken over 14 days, whereas 30 mg. given over three days is not lethal. This necessity for a cumulative effect greatly reduces the danger of accidental poisoning. Dogs weighing from 8 to 10 kg. survive single doses of 1 Gm. per kg. of body weight, and daily doses of 50 mg. administered over from 10 to 14 days without developing spontaneous hemorrhages.

For initial field trials dicoumarol was added to bait at the rate of 200 mg. per lb. dry weight. Prebaiting has proved to be unnecessary, for the poison is entirely acceptable to the wild rat. The most satisfactory technic so far evolved has been to ensure that the rodents have constant and free access to the poisoned bait. The amounts eaten gradually become less as the rats become weaker and die, but the baits should be left for some time to poison the migratory rats, which are the source of reinfestation. O'Connor claims that complete clearance can be achieved with dicoumarol more economically than by other methods. (Annotation, Lancet, 26 June '48)

* * * * * *

Constriction of the Mid-Thorax as a Means of Reflex Maintenance of Respiration During Barbiturate Narcosis: Depression of the respiration center with serious reduction in the rate and minute volume of breathing is commonly encountered in barbiturate intoxication. The sensitivity of the center to carbon dioxide is lost, or at best materially diminished, and respiration becomes largely, if not entirely, dependent upon reflex drives for its maintenance. Increase in the rate of breathing of dogs at this stage may be accomplished by compression of the chest, a maneuver initiating reflex drives involving proprioceptive impulses possibly from both the lung and the chest wall. The application of a constricting band about the mid-thorax as a means of eliciting and maintaining this effect is the subject of this report.

Spirometric recordings, using a Basal Metabolic Rate Unit connected to a tracheal cannula, were made for 11 dogs, each under varying degrees of sodium pentobarbital (Nembutal) narcosis. The dogs were anesthetized with initial intravenous doses of from 20 to 25 mg. of the drug per kg. of body weight. Subsequent doses of from 5 to 10 mg. per kg. were given at frequent intervals in order to obtain increasing depths of anesthesia. Constriction of the chest was accomplished by the inflation of a sphygmomanometer cuff encircling the mid-thorax.

The stimulating effect of inflation of the cuff upon breathing was immediate at all levels of respiratory depression. During light anesthesia from 20 to 30 mg. per kg., inflation of the cuff to various pressures increased respiratory rates slightly and resulted principally in reduction of tidal air volumes. As toxic levels of the drug of from 40 to 60 mg. per kg. were reached, breathing became abnormally slow, from 3 to 5 respirations per minute. Inflation of the cuff to pressures of from 18 to 24 mm. Hg. at this point resulted in prompt and significant increases in rates, from 10 to 15 respirations per minute. Tidal air volumes which had increased during the period of abnormally slow breathing were reduced by the constriction to only slightly less than those seen during light anesthesia without constriction, thus assuring adequate tidal gas exchanges. The net result was an increase in the minute volume by as much as 115 percent. Inflation of the cuff to pressures greater than 24 mm. Hg. reduced tidal air without further increasing the rate. Pressures of as little as 12 mm. Hg. increased the rate of breathing in some instances. Smaller pressures did not alter respiration. As greater levels of toxicity of from 60 to 70 mg. per kg. were reached, the respiratory minute volume was markedly reduced, principally by a great reduction in the tidal air. Constriction of the mid-thorax in this instance resulted in an increase in rate and a slight increase in minute volume, still not sufficient, however, to maintain the animals' oxygen requirements. The respiratory responses to the procedure were maintained in all experiments as long as the cuff was inflated, but promptly disappeared upon deflation.

The effects of constriction, as observed in these experiments, appear to be associated with the Hering-Breuer reflex.

Various chemical, noxious, and proprioceptive reflex mechanisms controlling respiration have long been known, and methods for their utilization during respiratory center depression have been proposed. The method as described here is simple, efficient, and nondamaging and is capable of increasing pulmonary ventilation during drug depression. In some experiments animals were able to tolerate the administration of larger doses of from 70 to 75 mg. per kg. of the drug during the application of the constricting pressure, but upon deflation of the cuff they lapsed into respiratory failure. Attempts made to revive such animals by reinflation of the constricting cuff or by artificial respiration were futile. These findings seem to indicate that the torso pressure maintained a volley of vagal nerve impulses to the respiratory center and thus increased the latter's resistance to drug toxicity.

As yet, sufficient data have not been accumulated for judgment of the efficacy of this maneuver in clinical cases of barbiturate overdosage. Preliminary observations made thus far seem to indicate that it is applicable in such cases. (Science, 9 July '48 - A. C. P. Bakos and W. L. Howell)

* * * * * *

The Administration of Antibiotic Preparations by the Aerosol Method: Many different types of equipment have been used to produce therapeutic aerosols. The

most commonly employed apparatus consists of a glass vessel called a nebulizer. A medicated solution placed within this vessel is made into a fine mist by a stream of air or oxygen which passes through the vessel and forces the liquid against a glass baffle. In a properly constructed unit the size of the majority of the particles produced will be in the range of from 0.5 to 2 microns. The optimal size of a particle for penetration into the smaller bronchioles and alveoli is approximately 1 micron. Larger particles will be deposited on the mucous membranes of the mouth, hypopharynx, trachea, and large bronchi. The tiniest particles are likely to be exhaled with the expired air. A number of commercial nebulizers have proved to be satisfactory; one of these is the vaponefrin nebulizer.

This presentation is concerned primarily with the administration of penicillin and streptomycin aerosols and their efficacy in diseases affecting the respiratory tract. Penicillin usually is dissolved in physiologic salt solution and is used in concentrations varying from 10,000 to 100,000 units per cubic centimeter. Crystalline penicillin in the form of the sodium or potassium salt is considered to be the most satisfactory preparation. Bryson and his co-workers were able to recover from the urine 60 percent of the penicillin administered by means of inhalation to normal healthy adults. Concentration of penicillin in the blood varies considerably, but values commonly fall between 0.05 and 0.10 units per cubic centimeter one hour after the inhalation of 50,000 units per cubic centimeter.

At the Mayo Clinic there has been considerable experience with streptomycin as an aerosol. Streptomycin hydrochloride has been used in concentrations varying from 0.025 to 0.1 Gm. per cubic centimeter of physiologic saline solution. Concentrations in the blood have been negligible and only minute quantities of the drug have been recovered from the urine.

On the basis of present knowledge at the Clinic, the use of the aerosol therapy of diseases other than those affecting the respiratory tract cannot be advocated. Although penicillin reaches the blood through the alveoli, the concentrations obtained vary, are uncertain, and dependent on the ability of the patient to inhale the drug. The absorption of streptomycin through the pulmonary circulatory system is almost nil. Hence, the administration of antibiotic aerosols cannot be recommended as a substitute for the parenteral administration of antibiotic preparations.

The chief merit of aerosol therapy lies in effects exerted by the topical application of the inhaled antibiotic preparations on the bronchial mucosa and the mixing of these drugs with purulent bronchopulmonary secretions. In the experience of the author and co-workers this is best illustrated in the treatment of purulent bronchiectasis in which the method is of particular value in the preparation of patients for lobectomy. In the first place, the parenteral administration of penicillin and streptomycin has not proved to be beneficial in a considerable number of cases of bronchiectasis. Injections of these drugs have not

materially reduced the volume of pulmonary secretions; it is usually impossible to recover any of these antibiotics from expectorated material; repeated cultures of the sputum after intramuscular injections have failed to reveal any significant alteration in the bacteriologic content of the sputum. On the other hand, after the inhalation of these antibiotics most of the Clinic patients have experienced a marked reduction in the volume of sputum. Furthermore, both penicillin and streptomycin can be demonstrated in the sputum in significant quantities several hours after inhalation has been discontinued. In many instances bacteria have been eradicated from the sputum by a course of therapy.

Cases of suppurative bronchiectasis were selected for this study of aerosol therapy because objective criteria were available. Only patients with definite bronchographic evidence of bronchiectasis were included. Many of these patients had not improved after treatment with postural drainage or the sulfonamides or after the parenteral administration of penicillin. Complete bacteriologic studies of sputum were obtained prior to treatment and twice a week during treatment. Inhalation therapy was continued for periods varying from several days to several weeks. Penicillin was given to all patients in daily amounts varying from 200,000 to 400,000 units. Streptomycin hydrochloride was given in those cases in which cultures revealed the presence of Gram-negative bacteria. It usually was given in combination with penicillin, and the daily dosage varied from 0.5 to 2.0 Gm.

Aerosol therapy was considered to be successful if the patients' daily volume of sputum could be reduced by 75 percent or more. Of approximately 150 patients treated, 60 percent responded satisfactorily to use of penicillin alone. Nearly 50 patients were treated with mixtures of penicillin and streptomycin, and the response to treatment was satisfactory in 90 percent of these patients.

The multiplicity of types of bacteria present often makes it difficult to determine the predominating organisms. The significant bacteria commonly encountered include such Gram-positive organisms as the pneumococci, both hemolytic and nonhemolytic streptococci, and staphylococci. The common Gram-negative bacteria include Escherichia coli, Hemophilus influenzae, Aerobacter aerogenes, and Klebsiella pneumoniae. On many occasions Gram-negative bacteria were not isolated from sputum cultures until after the patient had been treated with penicillin aerosol. Barach and others have pointed out that these Gram-negative bacteria apparently elaborate a "penicillinase" which interferes with the bacteriostatic effect of penicillin.

The determination of the sensitivity of specific organisms to penicillin or streptomycin is a most important feature of the bacteriologic study of bronchial secretions. When feasible such studies were carried out before and during aerosol therapy.

Certain limitations of aerosol therapy in the treatment of bronchiectasis should be pointed out. The bronchial dilatation of bronchiectasis is a permanent change, and the suppurative process is a complication of damage of the bronchial

tree. If the patients are not suitable for pulmonary resection, relapses may occur after cessation of therapy. Continued treatment on a modified scale is essential if improvement is to be maintained. With continued treatment, resistant bacteria are likely to appear in the bronchial secretions. Gram-negative bacteria are especially likely to become resistant to streptomycin. The development of resistance by bacteria may well account for some of the failures in aerosol therapy and makes the treatment of recurrent bronchorrhea more difficult.

The efficacy of aerosol therapy in other bronchopulmonary conditions depends on the extent to which susceptible bacteria are responsible for these conditions. In some cases of early lung abscess it seems to have value. In asthma and emphysema the use of antibiotic aerosols is helpful only when these processes are associated with bronchial infection which can be controlled by the inhalation of antibiotics. In general, the experience with antibiotic aerosols in these conditions at the Clinic has not offered promise. Certain patients with chronic bronchitis have been helped by aerosol therapy. Inhalation treatment in acute virus infections of the upper part of the respiratory tract is not recommended. However, in some instances in which respiratory infections have been followed by a chronic productive cough, a streptomycin-susceptible strain of Hemophilus influenzae has been demonstrated and streptomycin aerosol has proved to be very beneficial. In acute pneumonias, parenteral therapy appears to be preferable to the aerosol therapy. However, there are times when a combination of the two may be indicated.

It has been clearly demonstrated that streptomycin is a valuable drug in the treatment of tracheobronchial tuberculosis. Both the parenteral administration of streptomycin and streptomycin aerosols have been used extensively. The conclusion has been reached that the parenteral method is more effective in promoting the healing of these lesions. In view of the fact that streptomycin aerosol is purely topical in its effect, it is evident that an adequate concentration in the blood is necessary in the treatment of tuberculous bronchial disease. However, the combined use of both methods is probably advantageous in the treatment in many cases of tuberculous ulceration in the tracheobronchial tree. (M. Clin. North America, July '48 - A. M. Olsen)

* * * * * *

Studies on the Control of Acute Respiratory Diseases Among Naval Recruits: Since 1943, the Navy Department has been conducting a continuing program of evaluating methods of air sanitation for the control of acute respiratory diseases among recruits. Particular emphasis has been directed to the use of ultraviolet irradiation in barracks and other places of congregation. This report concerns the results of the first 4 years of this program.

In each of these years the admission rates for respiratory disease among groups of recruits that had been subjected to ultraviolet irradiation were quite

consistently lower than the rates among comparable control groups. Differences as great as from 20 to 25 percent were frequently observed. At certain times, however, only slight differences of doubtful significance were recorded.

It may reasonably be concluded, therefore, that ultraviolet irradiation has a partial effect on certain types of respiratory disease which occur among recruits. It will be necessary, however, to achieve considerably greater reduction in incidence before this procedure can be recommended for more general use. The results are felt to be sufficiently promising to warrant a continuing program of field research.

In one study the use of oiled floors and bedding for suppression of dust failed to result in a reduction of incidence rates during an epidemic of beta hemolytic streptococcal infections. Further studies are necessary before the value of this procedure can be adequately estimated.

The epidemiological observations made during these 4 years have shown the complexity of the problem. Numerous infections both of known and unknown cause have occurred in epidemic proportions. The epidemiological patterns have varied each year. The factors controlling the occurrence and extent of many of these epidemics are but poorly understood. The relative importance of air-borne transmissions of each of these infections as distinct from contact spread is not yet known in spite of intensive research conducted in recent years. It is felt that the eventual development of practical and effective control measures will depend largely upon advances in knowledge of the cause and spread of the diseases involved. Future field trials of particular control methods should be so designed that basic etiological and epidemiological observations may be accumulated concurrently. (Res. Proj. NM 005 008 (X-744) - T. L. Willmon et al.)

* * * * * *

A Lipid Anticoagulant from Brain Tissue - Physiochemical Characteristics and Action in Vitro and in Vivo: Dilution of a crude aqueous brain extract or of a suspension of its lipid (cephalin) fractions often improve their clot-accelerating power. This apparent paradoxical behavior of strong thromboplastic solutions has been frequently observed. Attempts to separate the clot-inhibiting from the clot-accelerating substances have only been moderately successful. However, in this study it has been possible to separate from brain tissue, by a suitable method of extraction, a heat labile inhibitor of blood coagulation, probably of a lipid nature and acting in vitro and in vivo as a powerful antithromboplastin.

Although this lipid inhibitor of blood coagulation has some similarities with that described by Chargaff, it has some dissimilarities in that it is extracted in the cold, is heat labile, and easily soluble in ether. It does not seem to be the same substance discussed by De Suto Nagy, for it has widely different chemical properties and mode of action. This inhibitor has greater potency than either of these other two substances.

The fluidity of circulating blood seems to be maintained by a balance between anticoagulant and coagulant factors in the blood and surrounding tissues. Whether or not this inhibitor or a similar one plays a role in maintaining this fluidity remains to be clarified by further work. Thromboplastic substances liberated from damaged tissues and blood cells disrupt this equilibrium and initiate the changes (first phase of coagulation) which lead to clotting. The natural antithromboplastin of the plasma slows the development of clotting by reducing the amount of thromboplastin available for the activation of prothrombin. An antithromboplastin substance has been extracted from the plasma with methanol; when the methanol extract is added to the plasma, it enhances its antithromboplastic activity. The lipid anticoagulant extracted from brain is also soluble in methanol and has, furthermore, a range of thermolability similar to that of the natural antithromboplastin of the plasma.

The necessity of a plasma cofactor for the development of the antithromboplastic effect of the lipid extract may explain why inhibitors and accelerators of coagulation may exist side by side in the tissues without neutralizing each other's action. The lipid inhibitor becomes an effective antagonist to its own thromboplastin only in the presence of a plasma cofactor. Further observations on the nature of this cofactor and the species preferential activity of the lipid inhibitor are being reported in greater detail elsewhere. The data already presented, however, serve to stress the necessity of avoiding the mixing of clotting reagents derived from different species. This is particularly applicable to thromboplastins and antithromboplastins, a precaution that has been stressed by the authors and others.

No direct correlation seems to exist between the effectiveness of heparin and the lipid inhibitor as tested in vivo and in vitro. Although heparin is the stronger anticoagulant, the fact that it is rapidly excreted or inactivated in vivo has seriously limited its clinical usefulness. The longer duration of the effect of an intravenous injection of the lipid anticoagulant when compared with that of heparin seems to make the lipid more suitable in the anticoagulant therapy of thromboembolic disease. (Proc. Soc. Exper. Biol. and Med., May '48 - L. M. Tocantins et al.)

* * * * * *

Possibility of Trichiniasis from the Walrus: In May, 1947, the State Serum Institute in Copenhagen received a request for help from Greenland where a mysterious epidemic had broken out. Some paratyphoid-like disease was suspected; trichiniasis had hitherto never been detected in Greenland. The institute sent Dr. N. B. Thorborg to investigate the epidemic on the spot, and he and his associates have now reported on their findings.

There were about 300 cases with 33 deaths between the beginning of January and the middle of May, 1947. The disease usually began gradually, with progressive lassitude, headache, pains in the limbs and trunk, and slight fever. In some

cases there was diarrhea, a sore throat, or some other catarrhal condition. Sometimes the onset was acute, with shivering and high fever, vomiting, and diarrhea. The temperature rose gradually to a considerable height and fell by lysis, usually remaining at 99° F. or so for a week or two before it fell to normal. Patients with slight cases were afebrile. In about 80 percent there was a rash, sometimes scarlatiniform, sometimes urticarial. There was edema of the face or limbs or of the whole body, and pain in various muscles was almost constant. About half the patients had gastro-intestinal symptoms. The cardiovascular system was often profoundly involved, and the many cases of sudden death were evidently due to myocardial failure. The severity varied widely in different parts of Greenland, the case-mortality being nil in some areas and up to 37 percent in one area. The age of the patients ranged from 2 to 63 years, and all of them were natives of Greenland. Transmission from man to man was not demonstrable.

The diagnosis of trichiniasis was confirmed by eosinophilia, by reactions to cutaneous tests with a trichina antigen, by serological tests of samples of blood sent to Denmark, and by the demonstration of numerous and already encapsulated trichina larvae in the muscles of a patient who had died after 3 months' illness. The pig could not be incriminated at all and only 32 of the patients had eaten dog within a month of the onset of the disease. It was noticed, however, that in most places the epidemic synchronized with the walrus season and the consumption of walrus meat. Trichinae were not found in any of the samples of walrus meat examined, but the circumstantial evidence against it was very strong. The white whale (Delphinapterus leukas) also came under suspicion. (Annotation, Lancet, 26 June '48)

* * * * * *

Posture and Blood Pressure: It is more than fifty years since Leonard Hill demonstrated that four-legged mammals would die from cerebral anemia if kept upright for a few days. Does the development of man from quadruped to biped partly explain why he is so subject to hypertension? Wald and his associates showed that when the normal person stands up the necessary adjustment of blood pressure takes place rapidly, largely within the first minute, and it is now generally agreed that orthostatic hypotension is due to inadequate functioning of the sympathetic nervous system. The effect of posture on the blood pressure, however, has not hitherto been fully investigated in a large series of normal people. Currens (Am. Heart J., April '48) has now studied this effect in 500 men and 500 women between the ages of 18 and 55 years, their average age being 33.2 years. The blood pressure was recorded in both the recumbent and the erect position. The upper limits of normality were set at 150/90 mm. Hg.

In this investigation, diastolic hypertension was observed in 5 percent of the men and 2.8 percent of the women in both the recumbent and erect positions; it was found in 0.8 percent of the men and 0.2 percent of the women in the recumbent

position only; and it was found in 6.4 percent of the men and 1.8 percent of the women in the erect position only. In other words, nearly twice as many men as women had a diastolic hypertension, but when it occurred only in the erect position it was almost four times as common in men as in women. Taking a change of 4 mm. Hg. in the diastolic pressure and 10 mm. Hg. in the systolic pressure as significant, the diastolic pressure rose in 48 percent and fell in only 12 percent when the person stood up. For the systolic pressure the findings were reversed: it rose in 3.7 percent and fell in 33 percent on standing. No appreciable change with posture was noted in the diastolic pressure in 40 percent of cases and in the systolic pressure in 63.5 percent. The pulse-rate rose in 95 percent of the entire group on standing, the average increase being 13.2 per minute in both men and women.

The question arises whether these findings provide a useful and simple test for assessing the probability of a person developing hypertension in later life. A careful follow-up over a long period would be necessary to determine this. If, as has been estimated, man spends from one half to two thirds of his life in the erect or semi-erect position, the effect of this on those with an imperfect autonomic nervous system may be considerable. Certainly the findings of Currens emphasize the importance of rest in the recumbent position in the treatment of hypertensive patients. (Annotation, Lancet, 26 June '48)

* * * * * *

Progress Report on Dental Research Project Concerning Chemical Nature of Human Enamel Protein: Knowledge of the chemical nature of human enamel protein is important to dentistry in that it is one of the basic requirements for better understanding of the processes involved in caries and its control. Earlier studies of human dental enamel have been handicapped by (a) insufficient quantities of enamel protein for study, (b) insufficiently specific or sensitive technics of quantitative measurement, and (c) lack of a clear-cut definition of enamel.

In this investigation a procedure has been developed for securing large quantities of enamel by (a) severing the crown portion of each tooth and embedding it in plaster; (b) mechanically removing the dentin, dentino-enamel junction area, and the inner layer of enamel which contains the tufts, spindles, and dentinal processes by the use of round steel burs and diamond stones; and (c) chemically removing the acquired cuticles or pellicles by immersion in 5 percent hydrochloric acid for 30 seconds.

The enamel crown of the tooth has been defined as consisting of three distinct parts: (1) the outer layer, which is commonly referred to as the enamel cuticle or Nasmyth's membrane and is considered to be a final product of amelogenesis; (2) the inner layer - that layer adjacent to the dentino-enamel junction which contains the tufts, spindles, and dentinal processes (extensions); (3) the enamel proper, which is the principal bulk of the

enamel and contains the enamel prisms, prism sheaths, interprismatic substance, and lamella.

Established colorimetric tests for determining quantitatively the nature of human enamel as defined have been employed.

Complete recognition was given to the enamel cuticle or Nasmyth's membrane existing as an entity in the adult erupted tooth. A dialytic method of demineralization was used, with double sheets of cellophane acting as the semipermeable membrane. The residuum was hydrolyzed in an acetylation flask with 20-percent HCl at from 125° to 130° C. for 6 hours, and then neutralized to a pH of 3.5 and diluted to volume with 0.1 normal HCl; after filtering it was ready for analysis. The quantitative tests used were for the amino acids, cystine, cysteine, methionine and phenylalanine. These were colorimetric tests using napthoquinone and nitro-prusside as the active agents. A Klett-Summerson photoelectric colorimeter with a #40 filter was used. (Accuracy of the tests are to .02 milligram.)

The results showed that the enamel contained no soluble protein of either diffusible or nondiffusible nature. The protein existing in the enamel proper contained less than 0.2-percent cystine, and that protein in the enamel cuticle had a cystine content of almost 1 percent. The methionine contents showed the protein of the enamel proper to be from 1 to 1.2 percent, and in the enamel cuticle 1.5 percent. The phenylalanine contents for both proteins were from 5 to 6 percent. The differences in the sulfur-containing amino acids, cystine and methionine, would indicate that the protein of the enamel proper and of the enamel cuticle are different and must be recognized and studied separately. The complete figures are being compiled to be reported on later. Also, duplicating of analyses are now under way to validate present findings and interpretations. (F. L. Losee, DC, USN and W. Hess of Georgetown University)

* * * * * *

Preparation of a Serological Antigen and a Vaccine for Experimental Tsutsugamushi Disease (Scrub Typhus): An antigenic suspension of Rickettsia orientalis was produced by the differential centrifugation of infected yolk sacs of embryonated hens' eggs. The purification was made possible by the use of casein hydrolysate as diluent.

The suspension used as the antigen in complement-fixation tests reacted specifically with sera from animals convalescent from experimental tsutsugamushi disease.

Mice inoculated intraperitoneally with the suspension showed a substantial immunity when challenged with 20,000 MLD of the homologous strain. The vaccine withstood lyophilization without loss of potency.

The heterogeneity of the serological pattern of various strains of R. orientalis was demonstrated by complement-fixation tests. Cross reactions with the various strains indicated the presence of common antigens in varying amounts depending upon the strain. (Proj. NM 005 002, (X-222), Rep. No. 9, 2 April '48, Nav. Med. Res. Inst., Bethesda, Md. - C. A. Bailey et al.)

* * * * * *

Three New Antimonial Compounds Active Against Experimental Infections with Schistosoma Mansoni: Three new antimonials, a sodium salt of p. sulfamido benzene stibonic acid (NMRI-501), a sodium salt of p. amido benzene stibonic acid (NMRI-896), and p. (sodium stibonate) ethyl benzoate (NMRI-889), were tested for their activity in the treatment of white mice infected by immersion with 300 cercariae of Schistosoma mansoni.

It was shown that, administered once daily for two weeks, NMRI-501 is superior in therapeutic activity to NMRI-896, NMRI-889, tartar emetic, and anthiomaline, and that it compares favorably with fuadin.

When administered twice daily for two weeks, NMRI-501 cured all surviving mice, showing it to be superior in therapeutic activity to fuadin and tartar emetic and equal in activity to anthiomaline. When injected twice daily for only seven days, however, the therapeutic effectiveness of NMRI-501 was markedly reduced.

The migration of schistosomes from the mesenteric veins to the liver during effective treatment was observed in these experiments. (Proj. NM 005 004 (X-535), Rep. No. 19, 21 April '48, Nav. Med. Res. Inst., Bethesda, Md. - J. H. Killough)

* * * * * *

List of Recent Reports on Naval Medical Research Projects:

Naval Medical Research Institute, NNMC, Bethesda, Maryland

Project	Report No.	Date	Title
NM 000 002	3	3 Feb '48	Studies on the Kinetics of Adsorption of Bacteriophage by Bacteria
NM 001 011	1	4 May '48	A Method for Continuous Recording of Gas Composition by Means of an Interferometer

Naval Medical Research Institute, NNMC, Bethesda, Maryland (Cont.)

Project	Report No.	Date	Title
NM 004 001	2	17 Mar '48	The Effect of Mechanical Vibration on the Patellar Reflex of the Cat
NM 005 004 X-535	15	18 Mar '48	Abnormalities in Development of Helminth Parasites with a Description of Several Anomalies in Cercariae of Digenetic Trematodes
NM 005 004 X-535	16	23 Mar '48	Metabolic Changes of Male and Female Schistosoma Mansoni During Growth
NM 005 004 X-535	17	25 Mar '48	A Rapid Method for the Determination of the Effect of Drugs on the Metabolism of Schistosoma Mansoni Using Warburg Technic
NM 005 004 X-535	18	1 Apr '48	The Effect of Sodium Salicylate on Experimental Schistosoma Mansoni Infections
NM 005 007	4	5 May '48	An Entomological Survey of Ponape, Eastern Caroline Islands
NM 005 009 X-754	2	23 Mar '48	Evaluation of a Pantothenic Acid Analogue (SN 14,622) as a Possible Antistreptococcal Agent
NM 007 007 X-539	7	9 Jun '48	The Action of Antimalarial Drugs in Mosquitoes Infected with Plasmodium Falciparum

Naval Medical Research Institute, NNMC, Bethesda, Maryland (Cont.)

Project	Report No.	Date	Title
NM 007 025	1	31 Mar '48	A New Instrument for Retracting the Walls of Blood Vessels to Facilitate Insertion of Artificial Tubes
NM 007 026	2	25 Mar '48	Studies on the Hyperglycemic Effect of Insulin
NM 007 039	7	26 Mar '48	Studies on the Toxicity and Anti-Heparin Action of Protamine in the Goat
NM 007 047	1	11 Mar '48	The Relationship Between the Fever Caused by Bacterial Pyrogens and the Fever of Acute Infections
NM 007 047	2	12 Mar '48	The Relationship Between the Fever Caused by Bacterial Pyrogens and the Fever Produced by the Intravenous Injection of Acute Sterile Exudates
NM 011 013	2	24 May '48	Preparation and Properties of Gallium Lactate
NM 011 015	4	23 Mar '48	Medical Aspects of the Texas City Disaster with Special Reference to the Effects of Air Blast
NM 011 015	5	1 Apr '48	A Method for the Routine Disinfection of Barbers Instruments Employing Two Quarternary Ammonium Compounds

Naval Medical Research Institute, NNMC, Bethesda, Maryland (Cont.)

Project	Report No.	Date	Title
NM 011 015	6	23 Apr '48	An Improved Radioactivity Measuring Cup

Medical Field Research Laboratory, Camp Lejeune, N. C.

NM 011 021 Sub-Proj. 1-48	-	4 Jun '48	Aerial Delivery of Medical Supplies by Parachute Drop
NM 011 021 Sub-Proj. 2-48	-	8 Jun '48	Field Testing of Hypo-Hone Hospital Kit, Needle Sharpener
NM 011 021 Sub-Proj. 3-48	-	2 Jun '48	Field Testing of Airborne Medical Equipment (Ward Beds)
NM 011 021 Sub-Proj. 4-48	-	4 Jun '48	Field Testing of Tent, Sectional Hospital
NM 011 021 Sub-Proj. 5-48	-	18 Jun '48	Field Testing of an Experimental Model Splint Set, Combat Pack Type

U.S. Naval School of Aviation Medicine and Research, NAS, Pensacola, Fla.

X-148 (Av-4-3)	18	25 Sep '47	Linear Acceleration and Deceleration as Factors Influencing Non-Visual Orientation During Flight.
X-148 (Av-4-3)	21	2 Jul '48	The Effect of Angular Acceleration on Sound Localization (The Audiogyral Illusion)
NM 001 019	1	3 Mar '48	Sunburn as a Cause of Temporary Lowering of Blackout Threshold in Flyers

NOTE: Those interested in seeing copies of the complete reports should address their request to the research activity from which the report originates.

* * * * * *

Change of Classification Regarding Naval Interns: In accordance with a recent administrative change, Naval interns are now being appointed as lieutenants (jg), Medical Corps, U. S. Naval Reserve and not lieutenants (jg), Medical Corps, U. S. Navy, for temporary service (internship). This method brings into uniformity the Army and Navy systems of commissioning officers who will be assigned to active duty under instruction as medical interns. It may be noted that through this change, certain advantages will accrue to those officers who are commissioned as lieutenants (jg), Medical Corps, U. S. Naval Reserve. These advantages will include reimbursement for travel of dependents and shipment of household effects to the officer's first permanent duty station; the $100.00 per month additional compensation provided by Public Law 365 - 80th Congress for officers commissioned in the Medical Corps of the United States Naval Reserve who volunteer and are accepted for extended active duty of one year or longer; an allowance of $250.00 for uniforms; and in case of disability or death in line of duty from disease or injury, the same pensions, compensation, retirement pay, and hospital benefits as are provided for officers of corresponding grades and length of service of the regular Navy. (Personnel Div., BuMed)

* * * * * *

Course in Aviation Medicine: The next course in Aviation Medicine will be given at the U. S. Naval Air Station, Pensacola, Florida, beginning 20 September 1948. This course of instruction has been lengthened to six months' duration to include additional subjects essential and peculiar to aviation and Naval needs.

Applications are desired from medical officers of the regular Navy in the ranks of lieutenant (jg), lieutenant, and lieutenant commander, who are interested in this specialty. No service agreement is required.

Applications are desired from Reserve Naval medical officers in the ranks of lieutenant (jg), lieutenant, and lieutenant commander, interested in this specialty who will sign an agreement not to resign during the course and to remain in the U. S. Naval Reserve for two years upon completion of their course.

Applications for this course may be made by dispatch and must reach the Bureau of Medicine and Surgery prior to 1 September 1948. (Professional Div., BuMed)

* * * * * *

Course on Diseases of the Chest: The Bureau of Medicine and Surgery has reserved 4 places for the postgraduate course on Diseases of the Chest which will be given at the Hotel New Yorker, New York City, under the sponsorship of the Council on Postgraduate Medical Education and the New York State Chapter of the American College of Chest Physicians. The course will be of 5 days' duration, beginning 8 November 1948 and ending 12 November 1948.

Requests are desired from medical officers of the regular Navy interested in this specialty. The cost of tuition will be borne by BuMed. Authorization orders only (travel, etc. at no expense to the U. S. Government) will be provided for medical officers selected to attend this course of instruction. No relief will be provided for medical officers attending. (Professional Div., BuMed)

* * * * * *

Extension and Acceleration in Medical Department Reserve Training Program: The Reserve Training Program acquires new importance based upon the retirement features of Public Law 810 - 80th Congress, 2nd Session (Approved 29 June 1948), Army and Air Force Vitalization and Retirement Equalization Act of 1948. Briefly, a Reserve officer may be retired at the age of 60 years provided he has completed an aggregate of 20 or more years of satisfactory Reserve service. He will then receive 2 and 1/2 percent of his active duty annual base and longevity pay multiplied by a number equal to the number of years of defined Reserve service in accordance with Title III, Sections 301 to 313 inclusive.

Subsequent to the enactment of this law, a year of satisfactory Reserve service shall consist of any year in which a person is credited with a minimum of 50 points, the points being credited on a specified basis of drill periods, active duty days (one point per drill and one point per day), 15 points for annual membership, and the remaining points built up by satisfactory completion of credited correspondence courses.

Now that retirement pay and promotion features will be intimately tied up with training, the Bureau of Medicine and Surgery is rapidly increasing its existing facilities for assisting and guiding the activities of the Volunteer and Organized Reserves. This broadened and accelerated activity in the Bureau's Reserve Training Program will extend to all categories of Medical Department Reserves, namely, the Medical Corps, the Dental Corps, the Medical Service Corps, the Nurse Corps, and the Hospital Corps including enlisted personnel.

* * * * * *

BUMED CIRCULAR LETTER 48-76 9 July 1948

To: All Ships and Stations

Subj: Procurement of Army Publications

Ref: (a) BUMED C.L. 44-57

1. Reference (a) is hereby canceled and superseded by this letter.

2. The list of Army publications published in Ref. (a) is obsolete and should not be used for ordering publications.

3. Medical Department activities may obtain Army publications by sending a written request to the Bureau of Medicine and Surgery, Navy Department, Washington 25, D. C. If an Army Publications Catalog is available these requests should give the Army catalog number, title, and date of publication.

--BuMed. C. A. Swanson

* * * * * *

BUMED CIRCULAR LETTER 48-77 12 July 1948

To: All Stations having Dispensaries or Dependents' Services

Subj: Services for Crippled and Handicapped Children

This letter (1) quotes, in part, a letter received by BuMed from the U. S. Children's Bureau of the Federal Security Agency which contains information of value concerning services available in the care of crippled or handicapped children who are dependents of military personnel and (2) requests addressees to report to BuMed any difficulty in obtaining services as outlined so that the matter may be taken up with the Federal Children's Bureau.

* * * * * *

BUMED CIRCULAR LETTER 48-78 14 July 1948

To: District Medical and Dental Officers

Subj: Addressograph Plates for Inactive Reserve Officer Personnel of the Medical Department; Maintenance of

Ref: (a) PERS-1D4-mmj, Serial F-738 ltr 27 April 1948 to Comdts., All NDs; Comdt, PRNC; and Chief, Naval Air Reserve Training.

This letter (1) contains certain instructions concerning the maintenance of addressograph plates for inactive Reserve officer personnel of the Medical Department and (2) requests that the District Medical and Dental Officer, upon the completion of the segregation of officers by corps and of the verification of addresses as outlined in reference (a), forward to BuMed an addressograph listing by corps.

* * * * * *

BUMED CIRCULAR LETTER 48-79 15 July 1948

To: MedOfCom, U. S. Naval Hospitals; National Naval Medical Center, Bethesda; Naval Medical Center, Guam; NavMed Supply Depots, Brooklyn, N. Y. and Oakland, Calif.

Subj: Civilian Personnel Administration in Medical Activities

Refs: (a) Manual of the Medical Department, Part I, Chapter 5, Paragraph 1512 and Part IV, Chapter 2.
(b) BuMed Circular Letter 47-118.
(c) Navy Civilian Personnel Instruction 125.

This letter (1) states that in accordance with Navy Civilian Personnel Instruction 125, the Bureau desires to adopt, within each addressed medical activity, an over-all program and uniform organization to execute civilian personnel functions; (2) states that owing to the nonindustrial nature of medical activities and the relatively small number of Medical Department civilian employees, it is considered that NCPI 125.5-1b is pertinent; (3) states that the particular purpose of this letter is to clarify and provide uniformity in existing instructions, particularly paragraphs 1512.1 to 1512.4 inclusive, of Part I, Chapter 5, of the Manual of the Medical Department, which are amplified by this letter; and (4) sets forth certain instructions for the accomplishment of (3) above.

* * * * * *